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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,040	07/19/2004	Hans H. Liao	6682-63358-09	7115

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EXAMINER

SLOBODYANSKY, ELIZABETH

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 12/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/502,040

Applicant(s)

LIAO ET AL.

Examiner

Elizabeth Slobodyansky, PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 November 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-67,69-74,76-81 and 89-107 is/are pending in the application.
- 4a) Of the above claim(s) 1-46,77-81 and 89-106 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 47-50,52,53,55-58,60-63,65-67,69-74,76 and 107 is/are rejected.
- 7) ☒ Claim(s) 51,54,59 and 64 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 July 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>7/19/04; 9/12/05; 1/10/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The amendment filed November 15, 2006 canceling claims 68, 75 and 82-88 and amending 2nd claim 106 to claim 107 has been entered.

Claims 1-67, 69-74, 76-81 and 89-107 are pending.

Election/Restrictions

Applicant's election with traverse of Group VIII, claims 47-67, 69-74, 76 and 107, SEQ ID NOs: 29 and 30, in the reply filed on November 15, 2006 is acknowledged. The traversal is on the ground(s) "Applicants disagree with the statement on page 4 (paragraph 8) of the Office action that states: "polypeptides having alanine 2, 3-aminomutase activity are known in the art." First, there is no art cited in the Office action to support this position. Second, this application contains the first disclosure of enzymes having alanine 2, 3-aminomutase activity. Therefore, the disclosed alanine 2, 3-aminomutase peptides and nucleic acids shown in SEQ ID NOS: 21, 21, 29 and 30 make a contribution over the prior art. The claims relate to a single general inventive concept under PCT Rule 13.1, because under PCT Rule 13.2, the special technical feature that is common to all of the claims are the novel alanine 2,3-aminomutase sequences provided by the application." (Remarks, page 15). This is not found persuasive because the polypeptides having alanine 2,3 aminomutase activity and polynucleotides encoding thereof are known in the prior art as can be seen from the rejection that follow. Furthermore, the scope of the claims is much broader than the specific sequences of SEQ ID NOs: 20, 21, 29, 30. The polypeptides encoded by SEQ

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ID NO:20 or SEQ ID NO:29 are mutated lysine 2, 3 aminomutases from different bacterial sources such as *Bacillus subtilis* and *Porphyromonas gingivalis* and have different structures. No common structure between these two polypeptides is disclosed as responsible for alanine 2,3-aminomutase activity. Therefore, they share no special technical feature.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-46, 77-81 and 89-106 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups I-VII, IX-XII there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on November 15, 2006.

Claim Objections

Claims 51-56 and 59-64 are objected reciting non-elected subject matter (SEQ ID NOS: 20, 21).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 47-50, 57, 58, 65-67, 69-74, 76 and 107 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 47-50, 57, 58, 65-67, 69-74, 76 and 107 are drawn to or depend from a polypeptide having alanine 2, 3 aminomutase activity and a nucleic acid encoding thereof. Thus, claims 47-50, 57, 58, 65-67, 69-74, 76 and 107 encompass the genus of polypeptides having alanine 2, 3 aminomutase activity and the genus of nucleic acids encoding thereof having undefined sequences. said polypeptides can be encoded by the same or different genes. Therefore, both the genus of polypeptides and the genus of nucleic acids are large variable genera comprising structurally different sequences both naturally occurring and man made.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure

of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant case, the specification discloses two polypeptides having alanine 2, 3 aminomutase activity of SEQ ID NOs: 21 and 30 that are encoded by SEQ ID NO:20 or SEQ ID NO:29, respectively. These alanine 2, 3 aminomutases are mutated lysine 2, 3 aminomutases from *Bacillus subtilis* and *Porphyromonas gingivalis*, respectively (specification, page 48, lines 27-28; page 49, lines 1-2). Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the “functionality” of being polypeptides having alanine 2, 3 aminomutase activity and nucleic acids encoding thereof and fails to provide any structure: function correlation present in all members of the claimed genus.

Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus.

Claims 47-50, 52-58, 60-63, 65-67, 69-74, 76 and 107 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide having alanine 2, 3 aminomutase activity of SEQ ID NO: 30 and a nucleic acid encoding thereof, including SEQ ID NO:29, does not reasonably provide enablement for a polypeptide having alanine 2, 3 aminomutase activity and a nucleic acid encoding thereof having no specifically defined sequences. It does not reasonably

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provide enablement for any cell producing 3-HP, 1,3-propanediol, pantothenate or CoA unless said cell comprises the required enzymes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The specification does not support the broad scope of the claims which encompasses polypeptides having alanine 2, 3 aminomutase activity and a nucleic acid encoding thereof both naturally occurring and man made having no specifically defined sequences. The specification does not teach said polypeptides and nucleic acids encoding thereof other than mutated lysine 2, 3 aminomutases of SEQ ID NOS: 21 and 30 and nucleic acids encoding thereof of SEQ ID NOS: 20 and 29, respectively.

The specification does not support the broad scope of the claims which encompass naturally occurring alanine 2,3 aminomutase as well as mutated lysine 2, 3 aminomutases having alanine 2, 3 aminomutase activity and having not specifically defined sequence because the specification does **not** establish: (A) regions of the protein structure which may be modified without affecting an alanine 2, 3 aminomutase

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activity either in a naturally occurring enzyme or in mutated lysine 2,3 aminomutases; (B) the general tolerance of polypeptides having alanine 2,3 aminomutase activity to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any alanine 2, 3 aminomutase or lysine 2,3 aminomutase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

With regard to claims 71-74, the specification enables only a cell comprising compounds such as enzymes that are necessary for conversion of β -alanine to 3-HP, 1,3-propanediol, pantothenate or CoA.

Without sufficient guidance, beyond that provided, obtaining a polypeptide having alanine 2, 3 aminomutase activity other than the polypeptide of SEQ ID NO:30 and a nucleic acid encoding thereof is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)).

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

the claimed invention is directed to non-statutory subject matter. Claim 47 is rejected as drawn to a polypeptide comprising alanine 2,3-aminomutase activity. Said polypeptide is

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a product of Nature and as such is unpatentable. Amending the claim to recite " an isolated polypeptide .." would obviate this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 47-50, 52, 53, 55-58, 60-63, 65-67, 69-74, 76 and 107 are rejected under 35 U.S.C. 102 (a, e) as being anticipated by Frey et al. (a) as evidenced by Frey et al. (b).

Frey et al (a) (US 6,248,874, form PTO-1449 filed 9/12/05) teaches lysine 2, 3 aminomutases and nucleic acids encoding thereof from different bacteria, including *Clostridium subterminale* strain SB4 (SEQ ID NOs: 1, 2, columns 4-5; claims). SEQ ID NO:2 of US 6,248,874 is 72.5% identical to SEQ ID NO:30 of the instant invention. SEQ ID NO:1 of US 6,248,874 is 37.9% identical to SEQ ID NO:29 of the instant invention. Subsequently, Frey et al (b) (US 20030113882-A1, form PTO-1449 filed 1/10/06) teaches alanine 2, 3 aminomutase activity of said polypeptide (pages 23-24, Example 5).

Furthermore, Frey et al. (a) teaches lysine 2,3 aminomutase from *Porphyromonas gingivalis* having the amino acid sequence that is 98.3% identical to SEQ ID NO:30 of the instant invention. It is encoded by a nucleic acid sequence that is 99% identical to SEQ ID NO:29 of the instant invention. The polypeptide of SEQ ID NO:30 of the instant invention and a polypeptide of SEQ ID NO:2 of US 6,248,874 have alanine 2, 3 aminomutase activity. Absent evidence to the contrary, lysine2,3 aminomutase from *Porphyromonas gingivalis* disclosed by Frey et al (a) has alanine 2,3 aminomutase activity.

Claims 47-50, 52, 53, 55-58, 60-63, 65-67, 69-74, 76 and 107 are rejected under 35 U.S.C. 102 (e) as being anticipated by Frey et al. (b).

Frey et al (b) teaches alanine 2, 3 aminomutase activity of a polypeptide from *Clostridium subterminale* strain SB4, *supra*.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

November 30, 2006